UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/768,183	01/23/2001	Jeno Gyuris	GPCI-P03-109	1943

28120 7590 05/28/2003

ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER
YU, MISOOK

ART UNIT	PAPER NUMBER
1642	19

DATE MAILED: 05/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/768,183	GYURIS ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-33,54-88 and 93-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-33,54-88 and 93-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Misook Yu.

DETAILED ACTION

Amendment (Paper No. 18) filed on 1-22-2003 is entered.

Claims 28-33, 54-88, 93-104 are pending and examined on merits.

Specification

The objection of the specification is withdrawn because applicant amended the specification for Fig. 5 with the amendment (Paper No. 11) and for Fig. 2 with the instant amendment (Paper No. 18).

Claim Objections

The claims objections are withdrawn because applicant argument that the specific limitations objected by the Office is not drawn to amino acid sequences but drawn to description of explaining protein structure is persuasive.

Claim Rejections - 35 USC § 112

Claims 28-33, 54-89 remain rejected and the new claims 93-104 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant argues that the claims are amended to avoid confusion and the specification at page 10 defines instant invention that albumin is carrier protein. These arguments are not persuasive because the argument does not specifically address the core problem associated of the limitation "increased biological activity": The claims say by inserting the peptide within serum albumin sequence enhance biological activity of the inserted peptide inherently, for example, if the biological activity of a peptide is a transferase activity, then the chimeric peptide inserted in serum albumin transfer something faster than the peptide itself without serum albumin. The prosecution history indicates that the Office rejected claims because specification does not teach any biological activity of a peptide increased other than serum albumin being used as carrier protein. WO 95/30759 (see

below in the art rejection) say that the purpose of inserting some therapeutically useful peptides is to increase plasma stability (in vivo half-life) of the therapeutically useful peptides. For the art search purpose of this Office, the Office will assume that that increased half-life is increased biological activity in view of applicant's argument that albumin is a carrier protein, which suggests has same meaning, i.e., increased plasma stability. However, this treatment does not relieve applicant the burden of responding to this rejection.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28, 54, 55-77, 93-104 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/30759 (Publication date Nov. 6, 1995, IDS AB filed on July 5, 2002, Paper No. 12) as evidenced by Zetter (1998, Annu Rev Med. Vol. 49, pages 407-24, abstract only) and by Fixe et al, Cytokine 1998 Jan;10(1):32-7.

The claims are interpreted as drawn to nucleic acid encoding a chimeric polypeptide comprising serum albumin (SA) with a useful heterologous peptide (H) inserted (claim 29), with insertion order SA-H-SA (claim 54), with insertion order N-terminal SA-H-C-terminal SA (claim 55), wherein the chimeric polypeptide exhibits increased biological activity, wherein the heterologous peptide is derived from an angiogenesis-inhibiting proteins (claim 56), from a protein or peptide fragments that binds to with various functional properties (claims 65-70), wherein the size of the heterologous peptide could be anywhere from 4 to 400 amino acids (claims 70-73, 93-104), wherein the tertiary structure of the chimeric polypeptide is similar to native serum

albumin (claim 74), wherein the inserted sequence replaces a portion of native SA sequence (claim 75), wherein the inserted peptide sequence and the replaced portion of native SA sequences are unequal length (claim 76), wherein all other claims list various useful proteins known in the art. By examination of the entire specification, it is the Office position that the inventors of the instant application did not discover any of the various therapeutically useful heterologous peptide listed in numerous claims or discovered unusual activity because of its insertion into serum albumin. The specification admits at pages 27-28 all of the useful peptide sequences listed in the numerous claims were known in the art before the effective filing date of the instant application.

WO 95/30759 teaches nucleic acid molecule encoding a chimeric polypeptide comprising serum albumin with a useful heterologous peptide inserted anywhere within serum albumin and a pharmaceutical composition wherein the useful heterologous peptide (with various peptide lengths) could be derived from various therapeutically useful protein including receptors, agonists, antagonists, an angiogenesis-inhibiting proteins (see "tumoral angiogenesis" at page 4 line 9), from a protein or peptide fragments that binds to trosine kinase receptor with various in vivo functional properties. See the entire article, especially abstract, page 1-5, last three lines of page 7 to line 7 of page 9, Fig. 1-6, pages 26-30, claims 1- 26. WO 95/30759 does not teach the functional properties of the heterologous peptide. It is the Office's position that WO covers any and/or every useful peptide known in the art by broadly listing at pages 3-4 and claims 3 and 4. WO 95/30759 also teaches the chimeric polypeptide comprising serum albumin increases in vivo stability and has other desirable pharmacological properties. See page 1. Although WO 95/30759 does not specify the functional properties of the various therapeutically useful proteins and peptides, the functional properties of the various therapeutically useful proteins or peptides listed at pages 3 and 4, and claims 3 and 4 are inherent properties of the various therapeutically useful proteins or peptides. However, Fixe et al (1998, Cytokine vol. 32-7, abstract only) et al present evidence: It is well known in the art before the effective filing date of the instant application that M-CSF is a tyrosine kinase receptor, therefore the biologically active

recombinant polypeptides essentially consisting of at least one active portion derived from M-CSF (see page 3 line 7 from the bottom of the page of WO 95/30759) inserted into an albumin would bind to a cell surface receptor protein (i.e., M-CSF-R), tyrosine kinase receptor (i.e., M-CSF-R), and to an extracellular domain M-CSF-R. Zetter (1998, Annu Rev Med. Vol. 49, pages 407-24, abstract only) further present evidence that angiostatin and endostatin are well known in the art as angiogenesis-inhibiting proteins useful for fighting cancer. Further, the instant specification at page 27-28 lists all the activities of hereologous peptides by incorporation to other references. See all the references listed at page 27-30 of the instant specification. Thus, WO 95/30759 anticipates claims 1-6, 8, 12-27, and 34

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-33 are rejected under **35 U.S.C. 103(a)** as being unpatentable over WO 95/30759 (Publication date Nov. 6, 1995, IDS AB filed on July 5, 2002, Paper No. 13) as applied to claims 28, 54, and 55 above, and further in view of the specification at pages 16-22.

The claims are drawn to delivery vector and transfected cells containing the chimeric peptides of the base claims 28, 54 and 55. The specification admits that the various vectors and cells are well known. Since the specification does not teach unexpected result using the recited vectors and/or cells, it is obvious variation of the vectors and cells taught by the primary references.

Claims 80-84 are rejected under **35 U.S.C. 103(a)** as being unpatentable over WO 95/30759 (Publication date Nov. 6, 1995, IDS AB filed on July 5, 2002, Paper No. 13) as applied to claims 28, 54, and 54 above, and further in view of Cardarelli et al, J Biol Chem 1992 Nov 15;267(32):23159-64.

The claims are drawn to insertion of at least two heterolgous peptides and claim 84 lists specific RGD peptide. The primary reference says that "at least one active" for example, at the abstract, therefore at least two of the instant invention, an obvious variant since the instant specification does not show a specific improvement or unexpected result over the prior art. Further, Cardarelli et al teach RGD is well known in the art.

Claims 85-88 are rejected under **35 U.S.C. 103(a)** as being unpatentable over PCT/FR95/00520 (AB of IDS, Paper No. 14, publication date: 11/16/1995) as applied to claims 28 above in view of Carter et al (1994, Advances in Protein Chemistry, vol. 45, pages 153-203, IDS AE filed on July 5, 2002, Paper No. 12). The claims are interpreted as drawn to nucleic acid encoding chimeric polypeptide comprising serum albumin with a useful heterologous peptide inserted into various recited serum albumin cysteine loops.

WO 95/30759 teaches that any therapeutically desirable peptide or polypeptide could be inserted into anywhere in the serum albumin polypeptides. See the claims rejection under 35 U.S.C. 102(b) above. WO 95/30759 does not specifically teaches that inserting any therapeutically desirable peptide or polypeptide into a cysteine loop or the heterologous peptide replaces a portion of a cysteine loop of a serum albumin protein although it teaches serum albumin has extensive cysteine loops. See Fig. 1 of WO 95/30759. However, Carter et al (1994, Advances in Protein Chemistry, vol. 45, pages 153-203) teach that crystal structure of serum albumin has been solved with high resolution, which shows that serum albumin has several surfaced exposed cysteine loops (see page 167-173). Since the specification does not teach any unexpected results with the specific cysteine loops, it is the Office position that the specific cysteine

loops are known in the art (those are not applicant's discovery) and it is obvious variation of the teaching of primary references.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 28-33, 54-84, 93-104 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 28-33, and 49-91 of copending Application No. 09/619,285. Although the conflicting claims are not identical, they are not patentably distinct from each other because products claimed in the instant claims are obvious variations because the products claimed in the base claims of the instant application includes the products of the copending application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
May 18, 2003

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600